Amendments to the Drawings

Please replace current Fig. 26 with replacement Fig. 26A and 26B attached hereto as **Exhibit A**.

Remarks

Claims 1-10, 14, 16-20, 24, 35-37 and 43-50 are pending. Applicant has hereinabove cancelled claims 1-10, 14, 16-20, 24, 44, 45, 48 and 52 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in the future. In addition, applicant has hereinabove amended claims 35, 36, 46, 47, 49, and 50, and added new claims 53 to 57. Support for the amendments to claim 35 can be found in the specification as originally filed at, inter alia, page 25, line 28 to page 26, line 4; page 26, lines 8-11; page 51, line 11; page 30, line 3; page 22, lines 26 to 29; page 24, lines 23-26; page 3, lines 7-10; page 29, lines 13-14; page 16, lines 28-29; page 17, lines 5-7; page 49, lines 25 - 27; page 76, lines 28-30; page 78, lines 9-10; and page 79, lines 19-23. Support for the amendments to claim 36 can be found in the specification as originally filed at, inter alia, page 4, line 34, to page 5, line 7 and page 21, lines 25-27. Claims 49 and 50 have been amended to correct for antecedent basis. Claims 46 and 47 have been amended to correct their dependency from claim 35. Support for the amendments to claim 52 can be found in the specification as originally filed at, inter alia, page 7, lines 1-4; and page 14, lines 14-17. Support for new claims 53 and 54 can be found in the specification as originally filed at, inter alia, page 25, line 28 to page 26, line 4; page 26, lines 8-11; page 51, line 11; page 30, line 3; page 22, lines 26 to 29; page 24, lines 23-26; page 3, lines 7-10; and at page 29, lines 13-14. Support for new claim 55 can be found in the specification as originally filed at, inter alia, Figs. 3a and 3F and the description thereof at page 8, lines 15-20; page 84, lines 11-16 and lines 17-20. Support for new claim 56 can be found in the specification as originally filed

at, inter alia, page 16, lines 30-34. Support for new claim 57 can be found in the specification as originally filed at, inter alia, page 49, line 30 and Fig. 31.

Applicant maintains that that the amendments to the claims raise no issue of new matter, and request entry of this Amendment.

Drawings

In the August 8, 2007 Office Action the Examiner stated that the drawings fail to comply with 37 C.F.R. §1.84(p)(5) because they do not include reference to Figs. 26(a) and 26(b) as recited in the specification.

In response, applicant has hereinabove amended the drawings to insert the identifiers (a) and (b) on Fig. 26. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this objection.

Specification

The Examiner asserted that the disclosure was objected to because the description of Figs. 30, 31, and 32 did not match Figs. 30, 31, and 32.

In response, applicant has hereinabove amended the Brief Description of the Figs. to correct this inadvertent error in Fig. labeling. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this objection.

Claim Objections

The Examiner objected to claim 35 as reciting the acronym CXCR4 without first defining it.

In response, applicant has hereinabove amended claim 35. Claim 35 does not now recite the term "CXCR4". Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this objection.

Obviousness-Type Double Patenting

The Examiner stated that claims 35-36 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 78-79, 83, and 85 of copending Application No. 10/512,518. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating a disorder of tissues involving loss or apoptosis of tissue cells comprising administering an agent effective to cause tissue cell proliferation within the tissue or to inhibit apoptosis of the cells within the tissue. The Examiner stated that claims 35 of the instant application recites that the agent induces activation of CXCR4 (which causes proliferation of the cells or inhibits apoptosis of the cells of the tissue). The Examiner stated that claim 36 of the instant application and claim 83 of the '518 application recite that the tissue is heart (cardiac) tissue. The Examiner also stated that claim 45 of the instant application and claim 79 of the '518 application both recite that the agent is stromal-derived factor-1.

The Examiner further stated that claims 35-37, 43, 45-49, and 51-52

are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 69, 77-78, and 82-84 of copending Application No. 11/234,879. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating a disorder comprising administering stromal-derived factor-1. The Examiner also stated that claim 35 of the instant application broadly recites treating a subject suffering from a disorder of a tissue involving loss or apoptosis of cells of the tissue comprising administering an agent which induces activation of CXCR4. Furthermore, the Examiner stated that claims 69 of the '879 application recites a method of increasing trafficking of endothelial progenitor cells to an ischemia-damaged tissue in a subject comprising administering stromal-derived factor-1 (which activates CXCR4). The Examiner stated that claims 45-49 and 52 of the instant application recite that the agent administered is stromal-derived factor-1α, stromal-derived factor-1ß, and stromal-derived factor-1γ. Additionally, the Examiner stated that, as indicated above, claim 69 of the '879 application recites administration of stromal-derived factor-1, and claims 77-78 further recite that the SDF-1 is SDF-1α and SDF-1ß. The Examiner stated that both sets of claims also recite that the tissue is heart tissue and that the SDF-1 is administered into the heart. The Examiner stated that both sets of claims also recite that the disorder or subject who is suffering has a myocardial infarction. Thus, the Examiner stated that the instant claims are not patentably distinct over the copending claims in Application No. 11/234,879.

The Examiner stated that these are provisional obviousness-type

double patenting rejections because the conflicting claims have not in fact been patented.

Applicants note that these are provisional rejections as the claims cited have not yet been patented. Accordingly, if this is the sole remaining ground of rejection, applicants respectfully request the Examiner to withdraw the rejection and allow the claims as amended to issue.

Claims Rejected Under 35 U.S.C. §112, First Paragraph (Written Description)

The Examiner stated that claims 35-37, 43, 49 and 51 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has hereinabove amended claim 35, from which the remaining rejected claims depend, to recite that the agent comprises human stromal derived-factor-1, as previously recited in dependent claim 45. Applicant maintains that claim 35 as amended hereinabove complies with the written description requirement. Applicant notes that the Examiner did not reject previously pending dependent claim 45 in the August 8, 2007 Office Action under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Furthermore, applicant notes that as amended, claim 35 recites that method comprises administering an agent comprising human stromal derived-factor-1 (SDF-1) wherein the human SDF-1 is human SDF-1α or human SDF-1β, which method the specification clearly describes such that one of ordinary skill in the art would

recognize applicant to be in possession of the claimed invention as of the priority date. The method is described at page 76, lines 28-30; page 77, lines 22-28; and page 78, lines 9-17. Moreover, the Examiner states on page 9 of the August 8, 2007 Office Action that a method using SDF-1 "meets the written description provision." Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Claims rejected Under 35 U.S.C. §112, First Paragraph (Enablement)

The Examiner stated that claims 35-37, 43, 45-49, 51 and 52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. The Examiner also stated that the specification is enabling for a method of treating a subject suffering from myocardial infarction comprising administering human stromal-derived factor-1α or 1β. The Examiner stated that the specification, while being enabling for a method of treating a subject suffering from myocardial infarction comprising administering human stromal-derived factor-1α or human stromal-derived factor-1ß, does not reasonably provide enablement for a method of treating a subject suffering from a disorder of a tissue involving loss or apoptosis of cells of the tissue which comprises administering to the subject an amount of an agent which induces activation of CXCR4 effective to cause proliferation of the cells or inhibit apoptosis of the cells of the tissue within the subject so as to thereby treat the subject.

The Examiner stated that there is little guidance in the instant specification indicating that any agent that activates CXCR4 (including SDF-1), can treat all possible disorders of a tissue involving loss or apoptosis of cells in the tissue. As discussed

above, the Examiner stated that the specification only discloses that administration of SDF-1 to rats with myocardial infarct results in an increase in neovascularization, a reduction in apoptotic cardiomyocytes, and an increase in cycling cardiomyocytes. However, the Examiner stated that this is not adequate, but it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The Examiner stated that the specification teaches that "'[t]issue' includes heart tissue and, in that embodiment, 'cells' include cardiomyocytes." The Examiner stated that "tissue" may also include lung, brain, gastrointestinal, liver, kidney and other tissues. The Examiner stated that "cells" also includes stem cells which can differentiate into the cell type being lost or progenitors of the cell type being lost in the disorder of the tissue. The Examiner stated that undue experimentation would be required of the skilled artisan to treat the numerous tissue disorders that involve loss or apoptosis of the tissue encompassed by the instant claims by administering all possible agents that activate CXCR4.

The Examiner also stated that the instant specification (page 21, lines 20-23) and claims 48 and 52 recite that one of the SDF-1 molecules to be administered is human SDF-1γ. The Examiner stated that at the time the instant invention was made, however, human SDF-1γ had not yet been discovered or characterized (see Yu et al. Gene 374:174-179, 2006). The Examiner stated that the specification provides no guidance to one skilled in the art as to how to obtain human SDF-1γ or that it has the functional activity required by the instant claims.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without

conceding the correctness of the Examiner's position, applicant has hereinabove amended claim 35, from which the remaining rejected claims depend, to recite that the method treats a subject suffering a disorder of a heart tissue and comprises administering an agent comprising human stromal derived factor-1 (SDF-1) wherein the human SDF-1 is human SDF-1α or human SDF-1β. In addition, applicants have hereinabove cancelled dependent claim 48 reciting human stromal-derived factor-1γ. Applicant maintains that such a method is enabled by the specification as originally filed. Applicants note that various disorders of the heart, as enumerated in the specification, cause loss of cells of the heart tissue. Applicants further note that the specification teaches that the administration of human stromal-derived factor-1 results in an increase in neovascularization, a reduction in apoptotic cardiomyocytes and an increase in cycling cardiomyocytes, as is acknowledged by the Examiner on page 11 of the August 8, 2007 Office Action. Moreover, as taught in the specification on page 79, lines 19-23; page 78, lines 22 to 23, and as supported by Fig. 26, the effects of SDF-1 administration are expected after an ischemic insult in the heart, i.e. not limited to myocardial infarction. Thus, one of ordinary skill in the art in possession of the specification would be able to make and use the invention as claimed in amended claim 35, and those claims dependent thereon. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims rejected Under 35 U.S.C. §102(e)

The Examiner stated that claims 35-36, 45-46, and 52 are rejected under 35 U.S.C. §102(e) as being anticipated by Peterson (U.S. 2002/0094327). The Examiner stated that Peterson teaches that

modulating the level of SDF-1α as protein in a target tissue can selectively direct migration of pluripotent stem cells to the target tissue (page 1, [0006]). The Examiner stated that Peterson continues to disclose that "[b]y increasing the number of pluripotent stem cells that traffic to the target tissue, the rate of tissue repair can be increased because there will be a greater number of pluripotent stem cells in the target tissue that can differentiate into cells which can repopulate and partially or wholly restore the normal function of the damaged tissue" (page 1, [0006]). The Examiner stated that Peterson teaches a method of targeting a pluripotent stem cell to a target tissue comprising introducing the SDF-1α protein into the mammalian subject in order to increase the concentration of SDF-1α in the target tissue (page 1, [0007]). The Examiner stated that Peterson teaches that target tissues can be any within a mammalian subject, such as heart (page 8, column 2, [0063]). The Examiner also stated that Peterson also discloses that target cells for use in the invention can include any cell in or that migrates to a target tissue (page 8, column 2, [0063]).

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has hereinabove amended claim 35, form which the remaining rejected claims depend, to recite, inter alia, that the method of treating a subject suffering from a disorder of a heart tissue comprises intramyocardially or intracoronarily administering to the subject an amount of an agent comprising human stromal derived factor-1(SDF-1) wherein the human SDF-1 is human SDF-1α or human SDF-1β. Applicant notes that Petersen does not teach such a method. Applicants further note that the Examiner has not suggested that

Peterson teaches such a method and did not reject previous claim 44, which recited intramyocardially or intracoronarily administering to the subject the agent, as anticipated by Peterson. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicant directs the Examiner's attention to the items listed below which are also listed on the Substitute PTO-1449 form attached hereto as **Exhibit B**. Copies of items 1-8 are attached hereto as **Exhibits 1-8**, respectively.

1. Hattori, Koichi et al. (2001) "Plasma elevation of stromal cell-derived factor-1 induces mobilization of mature and immature hematopoietic progenitor and stem cells" *Blood* 97:3354-3360 **(Exhibit 1)**

2. Lataillade, Jean-Jacques et al. (2000) "Chemokine SDF-1 enhances circulating CD34+ cell proliferation in synergy with cytokines: possible role in progenitor survival" *Blood* 95:756-768; **(Exhibit 2)**

3. July 29, 2005 Office Action issued in connection with U.S. Serial No. 10/128,738; **(Exhibit 3)**

4. March 27, 2006 Office Action issued in connection with U.S. Serial No. 10/220,554; **(Exhibit 4)**

5. March 27, 2002 Office Action issued in connection with U.S. Serial No. 09/587,441; **(Exhibit 5)**

6. January 2, 2002 Office Action issued in connection with U.S. Serial No. 09/587,441; **(Exhibit 6)**

7. September 19, 2001 Office Action issued in connection with U.S. Serial No. 09/587,441; **(Exhibit**

7) and

8. January 22, 2008 Office Action issued in connection with U.S. Serial No. 11/234,879. **(Exhibit 8)**

This Supplemental Information Disclosure Statement is being submitted under 37 C.F.R. §1.97(c)(2). Accordingly, applicant encloses a check in the amount of ONE HUNDRED AND EIGHTY DOLLARS for filing this Supplemental Information Disclosure Statement.

The Examiner is respectfully requested to make the listed items of record in the present application by initialing and returning a copy of the enclosed Substitute Form PTO 1449.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the total enclosed $705.00 fee, including a $525.00 fee for a three-month extension of time and a $180.00 Information Disclosure Statement fee, is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop Amendment
Commissioner for Patents
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Alexandria, VA 22313-1450

2/8/08

John P. White Date
Reg. No. 28,678

EXHIBIT A

EXHIBIT B